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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,699	06/14/2002	Ikuo Nishimoto	082376-000000US	2315

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EXAMINER	
LAMBERTSON, DAVID A	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 03/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,699	NISHIMOTO, IKUO	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-19* is/are pending in the application.

4a) Of the above claim(s) *3 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4-8,10-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 15, 2004 has been entered.

Claims 2-19 are pending in the instant application. Claims 3 and 9 are withdrawn as being drawn to a non-elected invention. Claims 2, 4-8 and 10-19 are under consideration in the instant application. Any rejection of record in the previous Office Action, mailed September 23, 2004, that is not addressed in this action has been withdrawn.

Priority

Applicant is reminded that the priority determination for the instant Application has been made only as far as the filing of PCT/JP00/06313 due to the absence of English translations of the foreign priority documents (see the Office Action mailed February 12, 2004).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

As it regards the instant maintained rejections, the Office wishes to clarify an interpretation of the claims in order to make clear the response to Applicant's traversal as it appears below. The claims as they are currently written contain the phrase "expressing in a cell a nucleic acid obtained from or synthesized from a nucleic acid obtained from a tissue of an organism suffering from a disorder, wherein said tissue is obtained from an organ showing cell death as a pathological feature of the disorder" (see for instance claims 2 and 8, specifically section (a)). Currently, the claim is interpreted where the active step is "expressing a nucleic acid in a cell;" thus, the nucleic acid is the feature of the claim that must have a functional effect in the claim. The portion of the phrase "obtained from or synthesized from a nucleic acid obtained from a tissue of an organism suffering from a disorder, wherein said tissue is obtained from an organ showing cell death as a pathological feature of the disorder" contains "reach-through" language as it regards the source of the nucleic acid to be expressed in the cell; in order for such language to carry patentable weight, there must be some structural or functional variation conveyed upon the nucleic acid as obtained from one source over another. In the absence of such a structural or functional variation, the nucleic acid as obtained from one source is functionally identical to a nucleic acid from any other source (i.e., a nucleic acid obtained from healthy brain tissue is the same as a nucleic acid obtained from a diseased brain tissue). Thus, with regard to this interpretation, the Office takes the position that, absent evidence to the contrary, the nucleic acids within a normal cell obtained from a normal tissue of a normal organ can also be obtained from a cell within the tissue of the same type of organ that suffers cell death because the cells all contain the same genetic material (i.e., the nucleic acids of a normal cell are the same as the nucleic acids of a cell from a tissue of an organ undergoing cell death). Thus, the

expression of a nucleic acid obtained from a normal cell is functionally the same as the expression of a nucleic acid obtained from a diseased organ, and are not patentably distinguishable. This point will also be further articulated in response to Applicant's traversal, below.

Claims 2, 4-8 and 10-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Vito *et al.* (IDS reference AG; see entire document; henceforth Vito). **This is a new rejection.**

Vito teaches the expression of a cDNA library in mice T-cell hybridoma (3DO) cells that are undergoing programmed cell death (PCD) induced by T-cell receptor (TCR) cross-linking (see for example page 521, left column, first paragraph). Vito further teaches the identification of six cDNA clones having a suppressive effect on the PCD phenotype of the 3DO cells, designated ALG-1 through ALG-6 (see for example page 521, left column second paragraph). It is important to note that the cDNA library is obtained from cells undergoing PCD, thus these nucleic acids are identical to those obtained from an organ undergoing cell death. Furthermore, as indicated in the interpretation of the claims, the cDNA molecules can be obtained from an organ suffering from cell death, absent evidence to the contrary. This includes brain and nerve tissue, as well as tissue isolated from Alzheimer's Disease afflicted organs.

Claims 2, 4-8 and 10-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Guo (as cited in the previous Office Action). **This rejection is maintained for the reasons set forth in the previous Office Action.**

Claim2, 4-8 and 10-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Giambarella (as cited in the previous Office Action). **This rejection is maintained for the reasons set forth in the previous Office Action.**

Response to Arguments Concerning Claim Rejections - 35 USC § 102

Applicant's arguments filed December 15, 2004 have been fully considered but they are not persuasive. Applicant provides the following grounds of traversal:

1. It is argued that the amendment of the claims to recite the phrase "showing cell death as a pathological disorder" delineates that organs recited in the claims from a normal organ, as most recently interpreted by the Office in view of the definition of "organ affected by a disorder" set forth on page 8 of the instant specification (see page 12, bottom paragraph of Applicant's response).

2. Applicant argues that the present claims are clearly distinguishable over the prior art because the Office has not shown that the nucleic acids disclosed in the references were obtained from a tissue obtained from an organ showing cell death as a pathological feature of a disorder (see page 13, first full paragraph of Applicant's response).

Applicant's arguments are not convincing for the following reasons:

1 and 2. It is important to note that the nucleic acid that is being expressed is the functional element of the claims (and therefore relevant element with regard to patentability). The difference between the organs is moot if the nucleic acids obtained from one organ are the same as the other, given that the claim calls for the expression of a nucleic acid in a cell. In other

words, unless there is some functional difference between the nucleic acids obtained from a normal organ and nucleic acids obtained from a diseased organ, the nucleic acids being expressed are the same. In both Guo and Giambarella, it is clear that the nucleic acids exhibiting a suppressive effect on apoptosis can be obtained from an organ undergoing cell death, given the source of the suppressor nucleic acid and absent evidence to the contrary.

The instant amendment contains "reach-through" type language regarding the nucleic acid recited the claim. The method step requires the expression of a nucleic acid in a cell, and indicates that the nucleic acid be obtained from a diseased organ. However, there is nothing in the claim to indicate that the nucleic acid obtained from a diseased organ has any structural or functional variation from a nucleic acid obtained from a normal organ. For example, gene X from a normal organ will be the same as gene X from a diseased organ, and this can be applied for every gene throughout the genome of the cells in any given organ. Furthermore, not all of the cells obtained from a diseased organ will even be characterized as diseased, as many cells in a diseased organ will have normal physiology. Indeed, the nucleic acids obtained from diseased organs will certainly contain nucleic acids from non-diseased cells, which would be identical to those obtained from normal cells. As such, it is clear that the nucleic acids obtained from normal cells read on the nucleic acids to be expressed in the instant claims. Since Guo and Giambarella express such nucleic acids in cells, Guo and Giambarella anticipate the instant claims even in view of the instant amendment.

Specifically, Guo overexpresses the calcium-binding protein calbindin D28k in neural cells, and finds that it has the ability to suppress mutant PS-1 induced apoptosis. Calbindin D28k is a gene that is expressed in cerebellar (brain) tissue, as presented by Nordquist (see for example

the previous Office Action, page 8, lines 3-6). There is nothing to suggest in the prior art or the instant specification that calbinidn-D28k is not expressed in cerebellar tissue from a brain undergoing cell death, thus this nucleic acid can be obtained from a tissue originating in an organ showing cell death as a pathological feature. Therefore, Guo teaches all of the limitations of the claims, given the "reach through" language.

Specifically, Giambarella overexpresses βARK1 in neuron-like NK1 cells, and finds that it has the ability to suppress apoptosis induced by the V642I mutant of the amyloid precursor protein (APP). The βARK1 gene originates in rat brain tissue, as presented by Arriza (see for example the previous Office Action, page 7, lines 9-12). There is nothing to suggest in the prior art or the instant specification that βARK1 is not expressed in a brain undergoing cell death, thus this nucleic acid can be obtained from a tissue originating in an organ showing cell death as a pathological feature. Therefore, Giambarella teaches all of the limitations of the claims, given the "reach through" language.

It is concluded that the nucleic acids taught by both Guo and Giambarella can be obtained from organs undergoing cell death as a pathological feature, given that the original source of both nucleic acids was the brain, and absent evidence to the contrary that these nucleic acids are not expressed in brains undergoing cell death. As such, Guo and Giambarella each teach the expression of a nucleic acid that can be obtained from an organ undergoing cell death, and the observation of a suppressive effect on cell death upon its expression in a host cell, thereby identifying a suppressor gene.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2, 4-8, 10-17 and 18-19* are rejected under 35 U.S.C. 103(a) as being unpatentable over Vito (as recited above in the rejection of claims 2, 4-8 and 10-17 under 35 USC 102(b)) in view of Slamon *et al.* (US 6,770,477; see entire document; henceforth Slamon). Note- * indicates the claims that are specifically rejected by the combination of references.

Vito teaches all of the elements as set forth above, specifically the expression of a library of nucleic acids in a cell, followed by the isolation of a plurality of nucleic acids having the ability to suppress the cell death phenotype of the cell. Specifically, Vito teaches the isolation of six cDNA clones having the ability to suppress the cell death phenotype. However, Vito does not teach the cross-hybridization of the six suppressors to identify which of the suppressors is non-redundant.

Slamon teaches the identification of 43 C clones and 36 H clones, and the cross-hybridization of these sequences to determine redundancy within the isolated clones prior to secondary screening (see for example column 47, lines 10-15). Following the cross-hybridization, 7 non-redundant C clones and 12 non-redundant H clones were identified (see for example column 47, lines 15-16). Thus, Slamon teaches that the use of cross-hybridization can be an effective tool in reducing the number of clones prior to further characterization.

It would have been obvious to combine the cross-hybridization technique of Slamon with the screening technique of Vito because both methods identify a plurality of clones that may be redundant in content, and Applicant clearly indicates that the use of such cross-hybridization techniques for the purpose of identifying non-redundant groups of nucleic acids was well-known to the skilled artisan prior to the filing date of the instant application (see for example page 9, second paragraph of Applicant's response). The skilled artisan would have been motivated to combine Vito and Slamon because it is desirable to reduce the number of clones to be further characterized to prevent redundant characterization of the same clone; as evident from Slamon, the cross-hybridization technique is useful in determining the unique members of a group of isolated clones, and this technique could be used to determine whether the ALG clones (1-6) are unique and require individual characterization, or if one or more clones is redundant, thus reducing the number of characterizations required for each of the unique clones. Absent evidence to the contrary, and given the well-known nature of the cross-hybridization technique for the purpose of identifying non-redundant groups of nucleic acids, the skilled artisan would have had a reasonable expectation of success by combining the Vito and Slamon references.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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